

NCI 2007 PRE-OP THERAPY IN BREAST CANCER
7 SESSION 1_5_KHOURI

DR. LAURA ESSERMAN: Our next speaker is Nagi Khouri, who is the director of breast imaging at Johns Hopkins University, and will be talking to us about evaluating the axilla and other nodal areas with non-invasive techniques.

DR. NAGI KHOURI: Thank you and good morning. The determination of the nodal status of breast cancer patients has a major impact on the therapeutic options available, namely, the need for lymph node dissection, and the option for preoperative chemotherapy prior to definitive surgery.

There is no reliable, non-invasive imaging method that can accurately predict the lymph node status. With the advent of sentinel node biopsy, only patients with a positive node need a lymph node dissection, therefore sparing a large number of women that procedure and the associated risk of lymphedema. It has also facilitated for women choosing the option of preoperative chemotherapy prior to definitive surgery.

In this discussion, we will focus on the contribution of ultrasound and fine needle aspiration biopsy of the draining nodes of the breast to the management of the patient with breast cancer. More specifically, we will address the question, under what circumstances could FNA replace the sentinel procedure without detriment to the patient?

We've looked at local extent of cancer. Dr. Lehman discussed it, with the evaluation of multi-focality, multi-centricity and the evaluation of the contralateral breast.

We are now going to be looking at the regional lymph node extension. And in the overall staging, we will always consider systemic extension -- this is not the scope of this lecture, but when we talk about CT scan, bone scan, and PET scan, it is usually done once the regional lymph nodes have been shown to be involved with the cancer and have been documented.

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When we talk about the draining nodes of the breast we talk particularly about the axillary nodes, the internal mammary nodes, the supra- and infra-clavicular and low cervical areas. Though there are articles that discuss the topic, all of them end up talking only about the axillary nodes. Very few articles mention the internal mammary nodes, and almost none mention the supra- and infra-clavicular and low cervical node evaluation. This is probably because we rarely do something surgically to the internal mammary nodes, at least in the U.S. And that might change, depending on the results from Dr. Veronesi.

So, very little data is published on internal mammary nodes, and therefore my discussion would really, almost exclusively, be directed to the axillary nodes.

But what is the status of what is done currently with patients with breast cancer, as far as the breast imagers are concerned? The majority adopt a “will not look” attitude, because they are not requested to do that. And therefore, they concentrate on the primary lesion in the breast. For those who do, ultrasound is the preferred method to look at the axilla, and the reports generally are very brief. They will mention whether there is or isn't a suspicious or a few suspicious nodes, without any further description.

The information nowadays comes also from MRI when it is done preoperatively as to nodes that need attention.

And there are few institutions that will perform needle biopsy -- mostly fine needle aspiration biopsy, rarely core biopsy.

If we think a little bit from a perspective point of view as to what is the distribution of cancer cells in the lymph node from metastasis, we can think of them as being isolated tumor cells; there could be islands of metastatic cancer; or a focal mass in one or multiple lymph nodes; or there can be total replacement of the node.

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And this is in a graphic illustration. You can see as the number and the distribution, as well as the size of the metastatic foci increases, so does the chance of a needle retrieving cancer cells in the specimen.

What are the sonographic criteria for indeterminate or suspicious metastatic nodes? Size is often talked about, but size alone is a very unreliable criterion, as we know. Morphological changes, on the other hand, are more reliable, and these are manifested by thickening of the cortex. It may be a diffuse thickening or an eccentric thickening. There may be lobulation of the cortex. The lymph node can, instead of being elongated, become rounded or vertically oriented. And, finally, there can be the complete disappearance of the hilum in this situation of the totally replaced lymph nodes. And in questionable areas, one can always look at the contralateral side. Overall, in a normal individual, the lymph nodes on the right side will be symmetric with the lymph nodes on the other side.

There are benign causes for enlargement of lymph nodes. One is normal. There is a lot of variation in the appearance of nodes in individuals. There can be hyperplasia or a reactive node, particularly after a recent biopsy, particularly if the biopsy has occurred more than three weeks prior to the evaluation with ultrasound. And then there are other systemic diseases that can account for adenopathy.

And these are examples, mixed examples, of patients with metastatic disease and reactive lymph nodes, all biopsy-proven. The first two on the left side are individuals who have palpable, grossly palpable, disease in the axilla – one retaining the normal architecture, and the second one being totally replaced. The nodes in the middle, the superior one, is a metastatic node, and the inferior one is what looks like a totally replaced lymph node in a woman who had a surgical biopsy about a month before she came to Hopkins. A fine needle aspiration biopsy showed only benign, reactive cells. Surgical excision showed

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that this was the case. The final node, the upper node on the right side, is metastatic with an eccentric lobulation of the cortex. And the one below middle image is a reactive lymph node.

So, really, morphologically, we cannot depend on the appearance of the node. This is, finally, another case -- a lymph node adjacent to a 2 cm cancer, eccentric bulge of the node, fine needle aspiration biopsy: reactive cells; final pathology: reactive cells.

This is a review of a large series of 16 studies evaluating the accuracy of sonography in the evaluation axillary lymph nodes. And you can see that the sensitivity of ultrasound in the detection, either by size only or size and morphology, varies quite a bit -- between 50 and 80 percent. The higher sensitivity alone, without intervention, is associated with a lower specificity. On the other hand, the addition of fine needle aspiration biopsy increases significantly the sensitivity as well as the specificity.

This is an interesting study from the University of Kentucky where they selected patients to undergo a fine needle aspiration biopsy. Basically, they selected patients that they called high-risk -- and I will define that in a second -- but clinically negative axilla. And 37 patients out of 114 patients qualified. And the criteria were a grade 3 tumor greater than 1 centimeter, plus or minus lymphatic invasion, or grade 2, more than 1.5 centimeter lesion.

And you can see that 22 patients with abnormal lymph nodes were identified, 68 percent of which had a diagnosis of cancer on fine needle aspiration biopsy. Out of the patients with a negative node [on FNA], the sentinel node showed cancer 3 in out of 7. And out of the 15 patients that had a negative axilla and no FNA, about 25 percent of those had a positive sentinel node.

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In total, out of the 22 that had metastatic disease on final histology, 64 percent had a grade 3, mean size 5 cm tumor, with lymphatic invasion in 50 percent, and a high rate of positive FNA. In the patients who had a negative evidence of lymph node metastases, 87 percent had a grade 2, mean size 3.2 cm, and lymphatic invasion very low -- about 8 percent.

From our own series at Hopkins, randomly selected for fine needle aspiration biopsy, we biopsied 69 axillae. 23 were clinical T1, and 32 were clinical T2. 41 were N0, 22 were N1. The remaining were higher, both T and N rating. Of those that were biopsied, about 41 patients, or 59 percent, had a positive FNA, 56 percent of which elected to have preoperative chemotherapy.

Out of the patients who had a negative FNA, 25 percent ended up having a positive sentinel lymph node. Therefore the sensitivity in that study was about 82 percent, and the specificity of about 100 percent.

Just to talk very briefly about some technical aspects of FNA of the lymph node. We use a 23-gauge needle -- in the literature it varies between 20 and 23.

It is important to sample the lymph node adequately, and that is one of the features of FNA -- is that we can move the needle quite a bit.

Biopsy the ventral, caudal, cephalad, and dorsal aspect, if feasible, of the lymph node. Avoid the hilum, because that gives you immediately some blood, and metastases tend to be cortically oriented.

Usually, we will aspirate three times -- either three passes of the same node, if there's only one node that is involved, or one pass of [each of] three separate nodes, if we think that three of the nodes are abnormal. Obviously, if the medical oncologist is interested in

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knowing exactly how many nodes and there are more nodes and they'd like them sampled, that can be done. Usually 30 to 40 excursions are done, and we stop when blood appears in the hub of the needle.

It's important for the radiologist to learn how to smear the slides and prepare for cytology. We do not need to have the cytopathologist present during this session.

From the point of view of logistics, both for the patient as well as for our surgeons and the medical oncologist, the ability to perform the FNA [of the axilla] at the time of the core biopsy [of the breast] plays a very significant role in making those results available at the time of the first interaction between the surgeon and the medical oncologist and the patient.

There are issues, unfortunately, to the widespread utilization of fine needle aspiration biopsy. First are the skills of axillary ultrasound performance as well as interpretation. Second, the skills of the performance of FNA – and I'll admit that the performance of FNA is a little more demanding than a core biopsy within the breast; but there is no reason why that could not be taught and learned. And finally, also very important, the skills of cytopathologic interpretation; and we do lack those in many institutions.

So, the impact of axillary ultrasound and FNA is that it has a reasonable sensitivity and a very high specificity. If the fine needle aspiration biopsy is positive for cancer, then the patient is a candidate for surgery and lymph node dissection [with no need for a sentinel node biopsy], or preoperative chemotherapy followed by surgery. If the FNA is negative for cancer cells, then the patient still needs a sentinel node performed. Thank you very much.